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Nutritional Aspects of Magnesium Metabolism

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The absolute necessity for magnesium in plant and animal nutrition is easily appreciated when one realizes that magnesium is found in high concentration in cells. It is necessary for photosynthesis in plants and for all reactions involving adenosine triphosphate in plant and animal cells. Although it is abundant in nature in general, deficiencies occur in both plants and animals. Human beings need about 5 mg of magnesium per kg of body weight per day. Infants and young children need twice as much. Children and women during pregnancy or lactation require significantly greater amounts than normal adults. Various diseases result in a deficiency of magnesium because of interruption of food intake or intestinal or renal wasting of the mineral.

IT WAS DISCOVERED that plants have an absolute need for magnesium (Mg) for growth when it was found in 1860 that plants raised on an entirely synthetic medium would not grow without this mineral. Magnesium protoporphyrin is an obligate part of the chlorophyll molecule, so that the entire chain of food and of fossil fuels has depended on its presence. Furthermore, magnesium has a vital role in all phosphate-dependent metabolic processes of plants and animals. Naturally occurring magnesium deficiencies in plants have been clearly documented in regions in which there is a low content of the mineral in the soil. For example, sand brown of tobacco was recognized in 1922. Subsequently, such deficiencies have been found in potatoes, apple trees and other plants. Magnesium deficiency is manifested by fading of the green color of leaves and by early defoliation. The Atlantic coastal plain between Maryland and Florida has many areas in which the soil has a marginal content of magnesium. The beneficial effects of using magnesium-enriched fertilizers were first shown in the 19th century; now such fertilizers are used to replenish soil found by chemical analysis to be depleted. Cattle raised on grass grown in soil that has a low Mg content are susceptible to the development of a magnesium deficiency. However, as mentioned above, this condition can be prevented by appropriate fertilization of the soil.

It was suspected that magnesium played an important role in animal nutrition even before it was proved conclusively by Leroy in 1926.[1] He was the first to show that mice stopped growing and later died when placed on a Mg-deficient diet. The need for magnesium in the growth of weanling rats is dramatically illustrated in Figure 1 (Griffith JA, Flink EB: Unpublished data, 1962). In 1932 Kruse, Orent and McCollum[2]

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ABBREVIATIONS USED IN TEXT

ATP = adenosine triphosphate
Mg = magnesium
TPN = total parenteral nutrition

conducted experiments—which are now considered classic—on magnesium deficiency in rats, by using a diet with 1.8 parts of Mg per million. Many other studies have followed. In some ways rats respond uniquely, particularly with regards to metabolism of calcium (Ca). Magnesium deficiency in rats results in significant aminoaciduria.[3] This accounts in part for their failure to thrive and grow. Young animals are more vulnerable to the effects of diets deficient in magnesium than are mature animals.

Spontaneous hypomagnesemia occurs in cattle, other ruminants and horses. In 1929 Sjollema[4] found hypomagnesemia in cattle, which usually occurs during the first few weeks of grazing in the spring, or after calving. The cows become restless, nervous and unsteady, have muscle twitching, grinding of teeth, rolling of the eyes and, finally, convulsions. It was called kopziekte by Sjollema which, unfortunately, was translated as grass tetany or grass staggers. A better literal translation would have been grass epilepsy, because tetany is not an accurate descriptor. This syndrome also develops in calves fed only milk for prolonged periods. In this instance the very high calcium content of milk competes with the much smaller amounts of magnesium for absorption. Young animals need much more Mg than mature animals. So too, infants, young children and pregnant or lactating women have much greater need for this mineral than other humans.

Biochemical Aspects

Some biochemical facts should help us understand certain vital aspects of magnesium metabolism. In photosynthesis magnesium is ionically bound in the center of the protoporphyrin molecule and apparently stabilizes the structure, so that it undergoes a perfectly reversible one-electron oxidation. The oxidation-reduction potential of chlorophyll correlates very well with the electronegativity of the central Mg ion. The chlorophyll molecule harvests light like a light meter.[5] The energy for synthesis of carbohydrate from carbon dioxide and water is derived from light

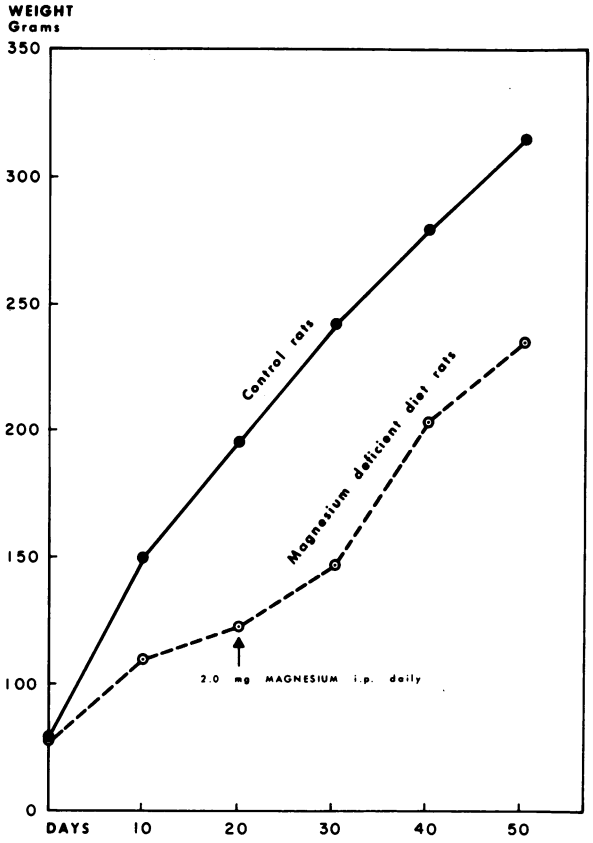

Figure 1.—Six weanling Sprague Dawley rats were given Purina Dog Chow, and six weanling rats were given a diet severely restricted in magnesium, which resulted in slow growth. Rats maintained on this severely deficient diet begin to lose weight after 20 days and all die within 30 to 40 days if left untreated. However, at 20 days, the six diet-restricted rats were injected intraperitoneally with 2.0 mg of magnesium (magnesium sulfate, $MgSO_4$). Treatment continued daily with obvious resumption of normal growth.

via chlorophyll and 12 separate enzymes catalyzed by adenosine triphosphate (ATP). Magnesium is a cofactor for ATP in all transphosphorylation reactions. It is a cofactor for many enzymes. In the absence of sunlight, plants use stored energy by way of oxidative phosphorylation. Animal cells, of course, derive their energy from oxidative phosphorylation which produces ATP. Phosphorylation in chloroplasts is light-dependent, but phosphorylation in mitochondria is dependent on oxygen and not on light.

The generation and use of ATP is dependent on magnesium—therefore, the synthesis of all proteins, including enzymes and hormones, nucleic acids, nucleoproteins, nucleotides, lipids and carbohydrates, as well as activation of formate, acetate and sulfate, transfer of methyl groups and muscle contraction. Magnesium acts to stabilize

ribosomes so that they do not dissociate into smaller particles and interrupt polypeptide synthesis. The size of RNA aggregates depends on optimum concentration of magnesium; therefore, polypeptide formation depends on magnesium as well.[5] The high concentration of magnesium and phosphate in cells is of obvious physiological importance.

Nutritional Requirements

Determining nutritional requirements for magnesium depends on analytical methods. At present the most precise method available is the one using atomic absorption spectrophotometry. The Perkin Elmer manual[6] describes details of such atomic absorption analyses. Important aspects of earlier techniques are discussed in detail by Alcock.[7] A great deal of knowledge has been gained by use of these somewhat less precise earlier quantitative methods.

A normal human conserves magnesium avidly as shown by several studies. Fitzgerald and Fourman[8] restricted the magnesium intake of two healthy men to 1.1 mEq per day for 22 days in one and 27 days in the other. The restricted diet resulted in a loss of 42 and 72 mEq of magnesium, respectively. No symptoms developed in either man and serum levels of Mg did not fall significantly. Shils[9] conducted a much more rigorous and prolonged study of dietary restriction in which only 0.7 mEq of magnesium per day was given for 42 to 117 days in six subjects and 266 days in one subject until pronounced symptoms developed. Levels of magnesium in the urine decreased to 1.0 mEq or less per day in all subjects within seven days. However, this drop occurred before there was significant decrease in serum levels of Mg. His elegant experiments illustrate the extraordinary ability of the kidneys to conserve magnesium. He also produced symptomatic magnesium deficiency that was fairly severe in some subjects by permitting no intake of the mineral for long periods. In his experiments all other nutrients were kept within adequate range so that no other form of malnutrition occurred.

Early techniques were cumbersome; however, over the years steady progress has been made in assessing nutritional requirements for magnesium in healthy subjects. Balance techniques, in use since 1915, are tedious and short testing periods can be somewhat misleading unless there is good agreement among the findings of all subjects involved in a given study. It is not surprising that there still are differing opinions about daily requirements. Certain factors adversely affect the magnesium balance in normal humans and in experimental animals. These include high levels of calcium, protein and phosphate.[10-12] A liquid protein diet recently popularized for weight reduction has been associated with serious metabolic consequences. This high nitrogen diet relative to other nutrients causes the depletion of magnesium.[13] Excessive alcohol intake is a very important factor in causing Mg deficiency as well. When any of these factors are present, more Mg is needed in the diet to maintain a necessary balance.

A study of a group of 16 normal adults and 11 obese adults on a metabolic ward was done.[14] An intake of magnesium of less than 3 mg per kg of body weight per day in the normal subjects and of 1.8 mg of magnesium per kg of body weight per day in obese subjects resulted in a slightly negative balance. However, an intake of 3.6 to 4.2 mg per kg of body weight per day in the normal adults and greater than 1.8 mg per kg of body weight per day in the obese adults resulted in a zero or positive balance. The total intake ranged from between 204 and 336 mg of magnesium per day. To attain higher intakes of Mg than this, persons eating typical American diets would have to consume more calories[15] or take Mg supplements.

In the subjects cited above who were receiving less than 144 mg of magnesium per day, 78 mg (58 percent of the intake) appeared in the urine per day. However, in those receiving more than 159 mg per day (range 159 to 288 mg), 45 percent of the intake was recovered in the urine, with a mean of 104 mg. Heaton[16] has shown a similar phenomenon. The absolute amount of magnesium absorbed and excreted by the kidney, therefore, is greater when the intake is high, so that the absolute amount absorbed correlates directly with the intake. In a study of young college women, a slight positive or zero balance of magnesium was maintained on an intake of approximately 260 mg of the mineral per day.[12] The addition of calcium or phosphate (or both) decreased the balance somewhat. In a summary of her review of the literature on balance studies in normal subjects, Seelig[17] concluded that the daily requirement of magnesium is not 300 mg per day or even 5 mg per kg of body weight per day, but probably at least 6 mg per kg of body weight per day. Others agree that this latter amount is needed by

adults.[18,19] It is clear that a definition of the ongoing need for magnesium is subject to variable interpretation. Except in rare cases of persons with renal wasting of magnesium, a zero or positive balance can be maintained by an intake of 4.0 mg per kg of body weight per day. Additional intake of magnesium may have beneficial effects, and this possibility is being investigated. The recommended daily allowances will be discussed below.

On an average, the amount of Mg excreted in the urine is 35 percent to 45 percent of the daily intake. The excretion into the urine of the radioactive isotope ^{28}Mg, which was administered to normal men without gastrointestinal tract abnormalities, was 41 percent ±8 percent.[20] This value corresponds very well with balance studies of normal subjects noted above. When ^{28}Mg was injected intravenously into a normal human subject, only 1.8 percent of the injected radioactive agent was recovered in the stool within 72 hours.[21] This agrees with nonisotopic studies too, namely that any excess magnesium after parenteral administration is not excreted in the feces but in the urine.

The magnesium content of food as calculated from tables of food composition and from chemical analysis shows that in a mixed general American diet it is very closely correlated with the total number of calories consumed.[15] This calculation breaks down, however, when an inordinate amount of calories is derived from refined sugars or alcohol, both of which contain neither magnesium nor other minerals. An important consideration regarding food intake is that refined sugar and processed food such as refined flour from wheat and polished rice from unpolished rice all lose a great deal of magnesium and calcium in processing.[19] This is a good reason for eating less refined foods, particularly whole cereal grains.

The Mg content of water may be of significance in nutrition. Magnesium and calcium are usually found together in hard water. Many studies of hard water versus soft water in different regions of the world have focussed on the relationship between hard water and, especially, its magnesium content and mortality from coronary artery disease. Such studies have been carried out in Australia, Belgium, Canada, Czechoslovakia, Finland, Holland, Ireland, Italy, Japan, Sweden, the United Kingdom, the United States, the USSR and West Germany.[19] There are widely differing points of view. In a recent study carried out in Hull and Burnley, England, the investigators found a greater mortality from coronary artery disease among persons living in the hard water region of Hull compared with those living in the soft water area of Burnley.[22] This finding is contrary to most studies, and a clear relationship between a "water factor" and cardiovascular health has not been established. However, as compared with regions in North America and the United Kingdom having hard water, in soft water areas cardiovascular deaths range from 15 percent to 76 percent higher.[19] Seelig and Heggtveitt[23] believe that the protective factor in hard water is more likely to be magnesium than calcium.

TABLE 1.—*Daily Nutritional Requirements for Magnesium*

Period of Life	*Age (years)*	*Daily Amount of Magnesium (mg/day)*
Infants	0-0.5	50
	0.5-1.0	70
Children	1-3	150
	4-6	200
	7-10	250
Males	11-14	350
	15-18	400
	19 and older	350
Females	11-14	300
	15 and older	300
	During pregnancy	300+150
	During lactation	300+150

The intake of magnesium and calcium is increased when hard water is used in cooking and as drinking water. This can make an otherwise marginal intake of Mg adequate. Theoretically, magnesium and calcium could also form insoluble soaps with saturated long-chain fatty acids and, thus, decrease the net intake of saturated fats from the diet. The solubility of these soaps is inversely related to the degree of saturation. (There is no scientific evidence for such a mechanism at this time, however.)

Actual nutritional requirements can be divided into two categories: (1) meeting the needs of normal humans for optimum nutrition and (2) meeting the needs of patients with overt or suspected magnesium deficiency to replenish the mineral until normal nutrition can be reestablished.

The 1980 recommended daily dietary allowances of the Food and Nutrition Board of National Academy of Sciences and National Research Council are recorded in Table 1.[24] These recommendations mean that a man weighing 70

kg (154 pounds) needs 5 mg per kg and a woman weighing 60 kg (132 pounds) also needs 5 mg per kg of body weight. Obviously, infants, young children and pregnant or lactating women need significantly more magnesium per day. Persons who weigh more than ideal weight eat more food and increase their intake of magnesium unless they eat mostly empty calories. Therefore, obese persons' nutritional requirements approximate the amount calculated on the basis of lean body mass. According to the magnesium content of a mixed diet (based on calculations from food table values and by chemical analysis), a diet of 2,500 kilocalories (kcal) should supply 300 mg of Mg and a diet of 3,000 kcal should supply 350 mg of this mineral. Obviously, the amount required for infants is two times or more that for adults. This permits optimum intake for rapid growth. A note of warning is needed regarding patients with chronic renal failure. The maintenance requirements are definitely less than those recommended above. It is necessary to monitor levels of magnesium from time to time in such patients.

TABLE 2.—*Causes of Magnesium (Mg) Deficiency*

Nutritional and Intestinal Causes (Inadequate Intake or Malabsorption)
Prolonged parenteral administration of fluid, including hyperalimentation without addition of Mg for three weeks or more
Chronic alcoholism
Severe prolonged diarrhea, ulcerative colitis, regional enteritis, chronic laxative abuse, villous adenoma or cancer of the colon
Intestinal Malabsorption:
• Short bowel syndrome due to extensive resection of small bowel, jejuno-colic fistula or gastrojejuno-colic fistula
• Gluten enteropathy (celiac disease and nontropical sprue)
• Tropical sprue
Starvation with attendant metabolic acidosis
Protein-calorie malnutrition including kwashiorkor
Diabetic ketoacidosis
Renal Causes
Diuretics, especially furosemide and ethacrynic acid, but also thiazides
Amphotericin B, gentamicin and gentamicin plus carbenicillin-induced renal tubular injury
Cisplatin-induced renal tubular injury
Renal tubular acidosis
Recovery from acute tubular necrosis (diuretic phase)
Chronic glomerulonephritis and pyelonephritis (rarely)
Familial and sporadic renal wastage of magnesium
Neonatal and Childhood-Associated Conditions
Infantile convulsions with hypomagnesemia and hypocalcemia
Newborns of diabetic mothers
Genetic (male) hypomagnesemia (specific malabsorption of Mg)
Exchange transfusions (citrate effect)
Congenital hypoparathyroidism
Infant born of mother with hyperparathyroidism
Endocrine and Metabolic Causes
Primary and secondary aldosteronism
Hyperthyroidism
Hyperparathyroidism with osteitis fibrosa cystica (particularly after parathyroidectomy)
Malacic bone disease (usually malignant lesions)
Excessive lactation
Last trimester of pregnancy

Magnesium Therapy and Supplementation

More magnesium is needed during periods of stress. Pregnant and lactating women need an additional intake of about 50 percent or more than the usual adult requirement. In one case, a lactating mother, who acted as a wet nurse as well as nursing her own child, produced a total of 2,400 ml of milk per day; tetany developed. Her serum magnesium level was 0.4 mEq per liter.[25] This extreme example highlights the clear need for greater intake of Mg during lactation.

The nutritional needs of patients vary according to the nature of the illness. Often magnesium is given for a short period to provide relief of symptoms; other times, continuing Mg supplementation may be needed if the illness is expected to be prolonged. Some of the special needs of patients with certain illnesses will be discussed below. Table 2 lists common and uncommon causes of overt magnesium deficiency to point out the variety of conditions in which there may be need for Mg therapy or supplementation.

Diabetes mellitus without acidosis results in loss of magnesium, thereby causing lowering of levels of serum Mg.[26] Diabetic ketoacidosis[27] is a state of acute starvation in a patient who may already be mildly depleted of magnesium before the onset of the ketoacidosis. The Mg deficit is usually moderate and may not require special therapy, but occasionally a severe deficit results and should be corrected by parenteral administration of magnesium. Patients with diabetes mellitus should receive more Mg daily than nondiabetic

subjects. Starvation was found to be associated with hypomagnesemia after World War II.[28] Total starvation leads to a continuous loss of Mg along with other nutrients including nitrogen and phosphate.[29] Vitamins and trace elements are also lost during starvation. The sudden termination of starvation by feeding protein and carbohydrate without cofactors can result in serious metabolic and neurological disturbances in spite of supplying therapeutic doses of the needed vitamins. Starvation victims of World War II who were fed too rapidly died, but the causative factors were not determined. Florid neuropathy occurs in some severely malnourished persons on refeeding even if thiamine is supplied.[30] Because of these clinical observations, Zieve[31] studied the problem and showed that magnesium deficiency in rats impairs the transketolase activity of the liver and of erythrocytes. In rats with both thiamine and Mg deficiency, thiamine repletion resulted in half as much increase in liver transketolase activity as during simple thiamine deficiency. The evidence is good that Mg deficiency interferes with the body being able to utilize thiamine. This observation is important in treating alcoholic patients in whom thiamine and Mg are severely depleted, such as those who have signs of the Wernicke-Korsakoff syndrome.

Serious Mg deficiency occurs in protein-calorie malnutrition of young children with marasmus or kwashiorkor in tropical areas primarily, but also in any region where severe malnutrition exists.[32-34] Patients who failed to respond to protein feeding and died were thought to have irreversible biochemical and pathological changes. Caddell ascribed this to Mg deficiency. Recovery is enhanced by addition of the mineral in large amounts.[33-37] Normally nourished and growing children require large intakes of magnesium. Therefore, in children with severe protein-calorie malnutrition, the need for replenishment to permit growth is even greater. It takes many days to correct the deficit.[37]

A magnesium infusion test, also called the Mg load test, has been used in infants to determine the presence of Mg deficiency, particularly in those in whom serum Mg levels are not very low.[34,36a,b] A 40-hour test was used to study magnesium and creatinine excretion before and after an intramuscular load of 0.49 mEq of magnesium per kg of body weight. No circadian variation of Mg excretion was detected, so a preload period of eight hours sufficed for baseline. Most of the excess magnesium was excreted by neonates by 32 hours and by infants from 1 to 6 months of age within 24 hours. Retention of 40 percent or more of the administered mineral was considered significant evidence of Mg deficiency. While this is an arbitrary determination, it is consistent with clinical observations.

Severe chronic alcoholism can be considered to be a form of adult starvation because empty calories have been taken in the form of alcoholic beverages instead of substantial food. The condition of these patients is similar to that of starved persons with regards to depletion of magnesium and other elements. Alcohol enhances the loss of Mg in the urine, so that intake of nutrients other than alcohol is interrupted and a renal loss results.[38-40] Several studies of electrolytes in muscles of chronic alcoholic patients or animals show significant depletion of magnesium, potassium and phosphate.[41,42] When refeeding takes place, Mg is retained avidly for six to ten days, after which equilibrium is usually reestablished. In persons unable to eat or who have pronounced Mg deficiency, parenteral administration of Mg is indicated.[43] Magnesium deficiency occurs regularly in chronic alcoholism, but its role in the development of symptoms is still an unsettled question. Clearly, magnesium should be administered parenterally if there is associated Mg-dependent hypocalcemia, cardiac arrhythmias or convulsions. I believe that parenteral Mg administration also is indicated in patients with Wernicke-Korsakoff syndrome and delirium tremens. After recovery, simple maintenance of a well-balanced, nutritious diet is sufficient.

Malabsorption and chronic diarrhea (from any cause) are the next most common medical causes of magnesium deficiency. These conditions include the short bowel syndrome, the closed loop syndrome, chronic ulcerative colitis and colon tumors that cause diarrhea.[44-46] As with most diseases, correction of the defect—in this case malabsorption or diarrhea—results in ending the wastage of Mg and the need for Mg supplementation. Ordinarily, in patients with the short bowel syndrome only partial correction of the condition is possible; thus, continued Mg supplementation will be necessary. The limiting factor of Mg therapy is diarrhea, which results from taking the mineral orally. Thus, when oral therapy does not suffice, often it is necessary to give Mg salts parenterally by the intramuscular route; occasionally, however, they must be administered intravenously at frequent

TABLE 3.—*Guidelines for Treatment of Magnesium (Mg) Deficiency*

1. It is important to determine that the kidneys are producing urine and that blood urea nitrogen and creatinine values are normal. Magnesium may be needed and may be administered even in the presence of severe renal insufficiency, but the treatment must be monitored by measuring serum or plasma levels frequently. Note that $MgSO_4$ (magnesium sulfate) is the heptahydrate $MgSO_4.7H_2O$. Ampules containing 1.0 gram of $MgSO_4$ or 8.1 mEq of magnesium are convenient to use. Parenterally given Mg doses recommended below refer to $MgSO_4$.

   General requirements: On the first day of therapy at least 1 mEq of Mg per kg of body weight (lean body mass) should be given parenterally. Subsequently, at least 0.5 mEq of Mg per kg of body weight per day should be given for three to five days. If parenteral fluid therapy continues after this, at least 0.1 mEq per kg per day should be given. Infants and young children need twice as much.

2. The following schedule for an average adult is safe and effective.

   Intramuscular route:
   - Day 1. 2.0 grams (16.3 mEq) every four hours for five doses.
   - Days 2-5. 1.0 gram (8.1 mEq) every six hours.

   Intravenous route (this is the preferred route if intravenous infusion is being used already):
   - Day 1. 5 grams (41 mEq) per liter of fluid and at least two liters or 82 mEq.
   - Days 2-5. A total of 6 grams (49 mEq) distributed equally in total fluids of the day.

3. For a sudden emergency such as convulsions or tachyarrhythmia.*

   Intravenous dose: 2 grams of $MgSO_4$ as 20 percent solution (10 ml of 20 percent $MgSO_4$) given in one minute. This should be followed by 5 grams of $MgSO_4$ in 500 ml solution over five to six hours and, finally, followed with the intramuscular schedule for days 2-5 as listed above.

4. Oral therapy. Most Mg salts can cause diarrhea, which can be a limiting factor (other preparations than the ones listed below can also be used).
   - Liquid milk of magnesia: one teaspoonful four times a day as tolerated, or
   - Magnesium hydroxide tablets: 300 mg tablet four times a day as tolerated; increase to two tablets four times a day as tolerated, or
   - Magnesium acetate (9.35 mEq per gram) as 10 percent solution: 10 ml in water four times a day as tolerated.

5. Monitor therapy. Magnesium repletion of tissues is slow. Magnesium levels need to be checked from time to time. As satisfactory blood levels are obtained, the dose can be adjusted to the lowest dose needed to maintain normal levels. Obviously, therapy should be stopped if the acute episode that caused the disturbance in first place has been corrected. Under certain circumstances, such as renal or gastrointestinal wasting of magnesium, the oral dose should be continued indefinitely.

*Adapted from Iseri.[53]

enough intervals to prevent overt symptoms of deficiency.

In adults the use of a magnesium load test has also been found to be useful in determining the presence of Mg deficiency. Although there is a circadian variation of magnesium excretion in normal subjects, this is not of sufficient magnitude to interfere with the use of a six-hour preload determination for basal Mg excretion. An intravenous injection of 33 mEq of Mg (4 grams of $MgSO_4$) in 1,000 ml of 5 percent glucose in water is given over six hours. All urine is collected for 36 hours, including during the period of infusion. Normal persons excrete all of the magnesium injected. More than 20 percent retention is considered to be clear evidence of deficiency.[41] Thoren[44] has described using a 24-hour urine collection and considers 20 percent to 25 percent retention of injected Mg to be evidence of a deficiency.

Certain renal diseases result in wastage of magnesium. Renal tubular acidosis, which also results in potassium and phosphate wastage is associated with Mg deficit. Rarely, patients are unable to conserve Mg, resulting in clinical manifestations such as intermittent convulsions, hypocalcemia and disturbed psyche. Siblings have been reported with chronic metabolic alkalosis and hypomagnesemia due to renal wastage of magnesium and potassium.[47] A male patient was discovered to have pronounced hypomagnesemia because of convulsions at age 5. He has been followed for several years now and can be kept reasonably asymptomatic, though hypomagnesemic, by administration of 100 mEq of Mg acetate per day. He excretes more than 30 mEq of Mg a day, indicating severe renal wastage of the mineral (W. E. Klingberg and E. B. Flink, unpublished data 1968). In rare cases, a male infant or a young male child has a defect of intestinal absorption of Mg. These children also have Mg-dependent hypocalcemia. This condition usually resolves itself with time.[48]

Administration of drugs to treat various diseases often results in Mg wastage and deficiency, which necessitates the additional intake of Mg. These drugs include amphotericin B, furosemide, ethacrynic acid, thiazide diuretics (to a lesser extent), gentamicin, carbenicillin[43] and cisplatin.[49] Cisplatin may cause damage to rental tubules, which persists long after cessation of therapy.[49] The loss may occur at a time when illness prevents the patient from receiving nutritious food as the

condition worsens. Prevention of a deficit is possible by prescribing oral Mg supplements in the amount that the patient can tolerate; often, however, parenteral therapy is necessary.

Total parenteral nutrition (TPN) has become a valuable adjunct for the management of critically ill patients who are otherwise deprived of nutrition. A need for potassium was assumed and this mineral incorporated into initial solutions. It was soon discovered, however, that magnesium had to be part of the daily infusion mixture as well, or signs and symptoms of Mg deficiency occurred within three to four weeks. Previously, it was felt that healthy persons not under abnormal stress could tolerate the absence of Mg for a longer period, but not for more than four to six weeks. Development of overt signs and symptoms means that considerable loss has already occurred. The serious consequences of phosphate depletion became apparent early in the last decade.[50] To prevent Mg deficiency in TPN-treated patients at least 8 mEq should be administered in infusion mixtures per day in an adult, beginning on the first day of treatment. In infants and young children the need is twice that for adults, or 0.2 to 0.3 mEq per kg of body weight per day for maintenance. Magnesium, potassium and phosphate often are depleted under the same circumstances of illness. Magnesium deficiency increases and perpetuates potassium deficiency in spite of adequate potassium intake.[51,52] Mg deficiency also enhances phosphate loss and deficiency.[41] Therefore, Mg is essential to insure retention of these other nutrients.

The nutritional needs of patients who are Mg-deficient already and who are acutely or chronically ill often can be met only by intensive therapy. Table 3 contains guidelines and useful suggestions for administration by parenteral and enteral routes.

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